REMARKS

This amendment is responsive to the first Office Action on this patent application, a continuation of U.S. Serial No.09/756,991, filed January 8, 2001, which is a divisional of U.S. Serial No. 09/338,179, filed June 22, 1999, which has since issued as U.S. Patent No. 6,222,030.

In the Action under reply, originally filed claims 1-30 have been examined. Applicants acknowledge with appreciation the Examiner's indication that claims 6-8, 12-17, 27 and 28 are allowable but for their dependence on rejected base claims. The remaining claims, i.e., claims 1-5, 9-11, 18-26, 29, and 30 stand rejected as follows:

(1) for obviousness-type double patenting over claims 1-4, 6-9, 13, 14, and 22 of U.S. Patent No6,222,030 to Dellinger et al. (claims 1-5, 9-11, and 29);

(2) under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 5,908,926 to Pirrung et al. (claims 1-3, 5, 18-26, and 29) ; and

(3) under 35 U.S.C. §103 as obvious over Pirrung et al. in view of U.S. Patent No. 5,705,621 to Ravikumar (claims 1-3, 5, 18-26, 29 and 30).

These rejections are addressed in part by the present amendment and Terminal Disclaimer Under 37 U.S.C. §1.321(c) and are otherwise traversed for the reasons set forth below.

Claim 1 as amended and claims 2-29 are pending.

THE CLAIM AMENDMENTS:

Claim 1 has been amended to emphasize that in contacting the coupled nucleoside monomer with an α-effect nucleophile, the following two events occur ***simultaneously***: (1) the carbonate protecting group is irreversibly removed; and (2) the phosphite triester linkage is oxidized to give a phosphotriester linkage.

Support for the amendment may be found in the specification at, for example, paragraphs 10 and 49.

THE DOUBLE PATENTING REJECTION:

Claims 1-5, 9-11 and 29 stand rejected under the judicially created doctrine of obvious-type double patenting as being unpatentable over claims 1-4, 6-9, 13, 14, and 22 of U.S. Patent No. 6,222,030.

In order to expedite prosecution, a Terminal Disclaimer in compliance with 37 CFR 1.321(c) is submitted with this response. Withdrawal of the double patenting rejection is thus in order and is respectfully requested by applicants.

§ 102(E) REJECTION - PIRRUNG ET AL.:

Claims 1-3, 5, 18-26, and 29 are rejected under 35 USC § 102(e) as being anticipated by Pirrung et al. The Examiner cites Pirrung et al. as describing a method for synthesizing DNA in the 5′ to 3′ direction in a manner analogous to that claimed by applicants. In fact, Pirrung et al. describes a method in which a nucleotide 3'-dimethoxybenzoin carbonate (DMB-carbonate) linked to a support (1) undergoes a tetrazole-mediated coupling reaction to add a second nucleotide, (2) is then treated with t-butylhydroperoxide or iodine/water/pyridine such that the new phosphite triester linkage is oxidized, and (3) is irradiated so that the carbonate protecting group is removed to give a free 3′-hydroxyl. Thus, in one step the oxidation of the phosphite triester is accomplished. Then in a later subsequent separate step, irradiation results in the presentation of a new 3' end for the next coupling, otherwise understood as deprotecting the moiety with irradiation (page 4 of the instant office action). It is the Examiner's position that the method of Pirrung et al. is identical to the method of claims 1-3, 5, 18-26, and 29 of the instant application. This rejection is respectfully traversed. In support of applicants' traversal, part (b) of claim 1 has been rewritten to emphasize that in the presently claimed method, the carbonate protecting group is irreversibly removed and the phosphite triester linkage oxidized ***simultaneously, in a single step***.

A claim is anticipated under 35 U.S.C. § 102 when each element of the claim is found in a single prior art reference. See, e.g., *Verdegaal Bros. v. Union Oil of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). It is well-established that if an independent claim is found allowable, all claims depending from that claim are also allowable. See, e.g., *Hartness International, Inc. v. Simplimatic Engineering Co.*, 819 F.2d 1100 (Fed. Cir. 1987). The independent claim at issue with respect to this rejection is independent claim 1, from which the other claims rejected under this section depend.

The broadest independent claim of the present application is claim 1. Claim 1, as currently amended reads as follows:

> 1. A method of synthesizing an oligonucleotide on a solid support comprising:

(a) coupling a nucleoside monomer having a protected hydroxyl group to a free hydroxyl group on a support-bound nucleoside monomer, wherein the hydroxyl group on the coupled nucleoside monomer is protected with a carbonate protecting group and the coupling reaction gives rise to a phosphite triester bond between the support-bound nucleoside monomer and the coupled nucleoside monomer;

(b) contacting the coupled nucleoside monomer with an alpha-effect nucleophile to simultaneously (i) remove irreversibly the carbonate protecting group, and (ii) oxidize the phosphite triester linkage to a phosphotriester linkage.

Step (b) of claim 1 has been amended to more clearly indicate the elements of the claimed method. The coupled nucleoside monomer is contacted with an α-effect nucleophile to simultaneously oxidize a triester linkage and remove the protecting group. On the other hand, Pirrung et al. oxidizes the triester linkage using an α-effect nucleophile, but in a second separate step facilitates a deprotection using irradiation. The claimed invention differs from Pirrung et al. in that the claimed invention presents simultaneous oxidation and deprotection steps. The present invention describes that contacting the composition with an α-effect nucleophile results in the oxidation of the phosphite triester linkage to a phosphotriester linkage and in simultaneous deprotection of the protection group. In addition, and significantly, the deprotection step is irreversible in the present invention.

The deprotection step in Pirrung et al. is reversible, and uses irradiation, not an α-effect nucleophile. More specifically, attention is called to the disclosure in Pirrung et al. on column 14, wherein the method steps are depicted schematically. In particular, it should be noted that the DMB protecting group remains on the molecule after the DIEA treatment step which oxidizes the ester linkage. In a subsequent step, after irradiation, the DMB protecting group is removed.

The amendment to claim 1 step (b) of the instant invention serves to clarify the steps taken in applicants' method in which deprotecting and oxidation happen simultaneously. Accordingly, the changes to claim 1 are not substantive changes, but rather reflect a rephrasing of the elements of step (b), fully supported by the disclosure in claim 1 as originally filed, to emphasize that the α-effect nucleophile acts to both oxidize the ester linkage and deprotect the protected moiety in a single step, and so to clearly indicate that the instant invention distinguishes over Pirrung et al.

As currently amended, claim 1 does not read on Pirrung et al. Accordingly, the claims of the present invention as amended do not read on Pirrung et al. and applicants respectfully request Examiner to withdraw her rejection.

§ 103(a) REJECTION - PIRRUNG ET AL. IN VIEW OF RAVIKUMAR

Claims 1-3, 5, 18-26, 29, and 30 are rejected under 35 USC § 103(a) as being obvious over Pirrung et al. in view of Ravikumar. Pirrung et al. has been cited as above, and Ravikumar has been cited as describing the step of cleaving a synthesized oligonucleotide from the support on which synthesis is carried out.

It is well settled in the law that there must be some reason for combining references other than the hindsight obtained from knowledge of the invention at issue as described in an applicant's specification. *See Interconnect Planning Corp. v. Feil*, 227 USPQ 543 (Fed. Cir. 1985).

The disclosure of Pirrung et al. pertains to the 5′ to 3′ synthesis of nucleic acids for the purpose of preparing arrays of oligomers bound to a support via their 5' ends. There is no motivation to combine the synthesis of Pirrung et al. with the cleavage of oligomers from a solid support of Ravikumar. As stated in Pirrung et al.: "the present invention provides a new approach to the photochemical synthesis of nucleic acids and to the preparation of high quality ***arrays of oligomers*** that permit the rapid analysis of genes, including those wherein mutations result in disease. The invention also provides new photochemically removable protecting groups that can be used in the present approach to nucleic acid synthesis," (column 2, lines 48-54) (emphasis added). Pirrung et al. does not describe synthesis of cleaved molecules or molecules that it might be desirable to cleave, but rather Pirrung et al. describes synthesis of arrays of oligomers attached to a substrate.

The specification of Pirrung et al. describes uses of arrays, the products of the methods claimed in the patent, and there is no discussion in Pirrung et al. of the opportunity of cleaving the newly generated oligomers from the substrate for other uses. Thus, a person of skill in the art would not be motivated to combine the cleavage methods of Ravikumar with the synthesis methods of Pirrung et al.

Accordingly, applicants respectfully request withdrawal of the rejection under 35 USC § 103(a).

OBJECTIONS TO THE CLAIMS:

Claims 6-8, 12-17, 27, and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all the limitations of the base claim and any intervening claims.

In view of the amendment to claim 1, and in view of the arguments above, applicants contend that claims 6-8, 12-17, and 28 are no longer be objectionable as being dependent on a rejected base claim. Accordingly, applicants respectfully request withdrawal of the objection to these claims.

CONCLUSION

With this paper, each of the Examiner's rejections and objections has been fully addressed and overcome. Because there will be no outstanding issues for this matter upon entry of this paper, applicants respectfully request withdrawal of all claim rejections and passage of this application to issue.

Any questions regarding this paper may be addressed to the undersigned attorney at 650-251-7707 or firestone@reedpatent.com.

Respectfully submitted,

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